## Sequence Listing

- <110> Goddard, Audrey
  Godowski, Paul J.
  Gurney, Austin L.
  Hillan, Kenneth J.
  Polakis, Paul
  Smith, Victoria
  Wood, William I.
  Wu, Thomas D.
  Zhang, Zemin
- <120> COMPOSITIONS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF TUMOR
- <130> P5002R1
- <140> US 09/888,257
- <141> 2001-06-22
- <150> US 60/063,540
- <151> 1997-10-28
- <150> US 60/089,653
  - <151> 1998-06-17
  - <150> US 60/099,792
  - <151> 1998-09-10
  - <150> US 60/103,678
  - <151> 1998-10-08
  - <150> US 60/235,451
  - <151> 2000-09-26
  - <150> PCT/US99/12252
  - <151> 1999-06-02
  - <150> PCT/US99/20111
  - <151> 1999-09-01
  - <150> PCT/US00/04342 ·
  - <151> 2000-02-18
  - <150> PCT/US00/05841
  - <151> 2000-03-02
  - <150> PCT/US00/08439
  - <151> 2000-03-30
  - <150> PCT/US00/23328
  - <151> 2000-08-24
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  - <151> 2000-12-01
  - <150> PCT/US01/06520
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| Lys               | Thr | Ser | Ser | Tyr<br>35  | Val | Gly  | Ala | Ser         | Ile<br>40  | Val | Thr | Ala | Val | Gly<br>45  |
| Phe               | Ser | Lys | Gly | Leu<br>50  | Trp | Met  | Glu | Cys         | Ala<br>55  | Thr | His | Ser | Thr | Gly<br>60  |
| Ile               | Thr | Gln | Cys | Asp<br>65  | Ile | Tyr  | Ser | Thr         | Leu<br>70  | Leu | Gly | Leu | Pro | Ala<br>75  |
| Asp               | Ile | Gln | Ala | Ala<br>80  | Gln | Ala  | Met | Met         | Val<br>85  | Thr | Ser | Ser | Ala | Ile<br>90  |
| Ser               | Ser | Leu | Ala | Cys<br>95  | Ile | .Ile | Ser | <u>V</u> al | Val<br>100 | Gly | Met | Arg | Cys | Thr<br>105 |
| Val               | Phe | Cys | Gln | Glu<br>110 | Ser | Arg  | Ala | Lys         | Asp<br>115 | Arg | Val | Ala | Val | Ala<br>120 |
| Gly               | Gly | Val | Phe | Phe<br>125 | Ile | Leu  | Gly | Gly         | Leu<br>130 | Leu | Gly | Phe | Ile | Pro<br>135 |
| Val               | Ala | Trp | Asn | Leu<br>140 | His | Gly  | Ile | Leu         | Arg<br>145 | Asp | Phe | Tyr | Ser | Pro<br>150 |
| Leu               | Val | Pro | Asp | Ser<br>155 | Met | Lys  | Phe | Glu         | Ile<br>160 | Gly | Glu | Ala | Leu | Tyr<br>165 |
| Leu               | Gly | Ile | Ile | Ser<br>170 | Ser | Leu  | Phe | Ser         | Leu<br>175 | Ile | Ala | Gly | Ile | Ile<br>180 |

Leu Cys Phe Ser Cys Ser Ser Gln Arg Asn Arg Ser Asn Tyr Tyr 185 Asp Ala Tyr Gln Ala Gln Pro Leu Ala Thr Arg Ser Ser Pro Arg 205 200 Pro Gly Gln Pro Pro Lys Val Lys Ser Glu Phe Asn Ser Tyr Ser Leu Thr Gly Tyr Val 230 <210> 7 <211> 432 <212> PRT <213> Homo Sapien <400> 7 Met Leu Gln Asp Pro Asp Ser Asp Gln Pro Leu Asn Ser Leu Asp Val Lys Pro Leu Arg Lys Pro Arg Ile Pro Met Glu Thr Phe Arg Lys Val Gly Ile Pro Ile Ile Ile Ala Leu Leu Ser Leu Ala Ser Ile Ile Ile Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe Pro Glu Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr Leu Gln Val Leu Asp Ser Ala Thr 110 Gly Asn Trp Phe Ser Ala Cys Phe Asp Asn Phe Thr Glu Ala Leu 125 130 Ala Glu Thr Ala Cys Arg Gln Met Gly Tyr Ser Arg Ala Val Glu Ile Gly Pro Asp Gln Asp Leu Asp Val Val Glu Ile Thr Glu Asn 155 Ser Gln Glu Leu Arg Met Arg Asn Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His Cys Leu Ala Cys Gly Lys Ser Leu 185 190 Lys Thr Pro Arg Val Val Gly Glu Glu Ala Ser Val Asp Ser 200 205 210 Trp Pro Trp Gln Val Ser Ile Gln Tyr Asp Lys Gln His Val Cys Gly Ser Ile Leu Asp Pro His Trp Val Leu Thr Ala Ala His

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| Gly                              | Ser            | Asp | Lys   | Leu<br>260 | Gly | Ser | Phe | Pro | Ser<br>265 | Leu | Ala | Val | Ala | Lys<br>270 |
| Ile                              | Ile            | Ile | Ile   | Glu<br>275 | Phe | Asn | Pro | Met | Tyr<br>280 | Pro | Lys | Asp | Asn | Asp<br>285 |
| Ile                              | Ala            | Leu | Met   | Lys<br>290 | Leu | Gln | Phe | Pro | Leu<br>295 | Thr | Phe | Ser | Gly | Thr<br>300 |
| Val                              | Arg            | Pro | Ile   | Cys<br>305 | Leu | Pro | Phe | Phe | Asp<br>310 | Glu | Glu | Leu | Thr | Pro<br>315 |
| Ala                              | Thr            | Pro | Leu   | Trp<br>320 | Ile | Ile | Gly | Trp | Gly<br>325 | Phe | Thr | Lys | Gln | Asn<br>330 |
| Gly                              | Gly            | Lys | Met   | Ser<br>335 | Asp | Ile | Leu | Leu | Gln<br>340 | Ala | Ser | Val | Gln | Val<br>345 |
| Ile                              | Asp            | Ser | Thr   | Arg<br>350 | Cys | Asn | Ala | Asp | Asp<br>355 | Ala | Tyr | Gln | Gly | Glu<br>360 |
| Val                              | Thr            | Glu | Lys   | Met<br>365 | Met | Cys | Ala | Gly | Ile<br>370 | Pro | Glu | Gly | Gly | Val<br>375 |
| Asp                              | Thr            | Cys | Gln   | Gly<br>380 | Asp | Ser | Gly | Gly | Pro<br>385 | Leu | Met | Tyr | Gln | Ser<br>390 |
| Asp                              | Gln            | Trp | His   | Val<br>395 | Val | Gly | Ile | Val | Ser<br>400 | Trp | Gly | Tyr | Gly | Cys<br>405 |
| Gly                              | Gly            | Pro | Ser   | Thr<br>410 | Pro | Gly | Val | Tyr | Thr<br>415 | Lys | Val | Ser | Ala | Tyr<br>420 |
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| Ile                              | Ser            | Gly | Arg   | His<br>35  | Ser | Ile | Thr | Val | Thr<br>40  | Thr | Val | Ala | Ser | Ala<br>45  |
| Gly                              | Asn            | Ile | Gly   | Glu<br>50  | Asp | Gly | Ile | Leu | Ser<br>55  | Cys | Thr | Phe | Glu | Pro<br>60  |
| Asp                              | Ile            | Lys | Leu   | Ser<br>65  | Asp | Ile | Val | Ile | Gln<br>70  | Trp | Leu | Lys | Glu | Gly<br>75  |
| Val                              | Leu            | Gly | Leu   | Val<br>80  | His | Glu | Phe | Lys | Glu<br>85  | Gly | Lys | Asp | Glu | Leu<br>90  |

| Ser                          | Glu           | Gln | Asp  | Glu<br>95  | Met | Phe | Arg | Gly | Arg<br>100 | Thr | Ala | Val | Phe | Ala<br>105 |
|------------------------------|---------------|-----|------|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|
| Asp                          | Gln           | Val | Ile  | Val<br>110 | Gly | Asn | Ala | Ser | Leu<br>115 | Arg | Leu | Lys | Asn | Val<br>120 |
| Gln                          | Leu           | Thr | qaA  | Ala<br>125 | Gly | Thr | Tyr | Lys | Cys<br>130 | Tyr | Ile | Ile | Thr | Ser<br>135 |
| Lys                          | Gly           | Lys | Gly  | Asn<br>140 | Ala | Asn | Leu | Glu | Tyr<br>145 | Lys | Thr | Gly | Ala | Phe<br>150 |
| Ser                          | Met           | Pro | Glu  | Val<br>155 | Asn | Val | Asp | Tyr | Asn<br>160 | Ala | Ser | Ser | Glu | Thr<br>165 |
| Leu                          | Arg           | Cys | Glu  | Ala<br>170 | Pro | Arg | Trp | Phe | Pro<br>175 | Gln | Pro | Thr | Val | Val<br>180 |
| Trp                          | Ala           | Ser | Gln  | Val<br>185 | Asp | Gln | Gly | Ala | Asn<br>190 | Phe | Ser | Glu | Val | Ser<br>195 |
| Asn                          | Thr           | Ser | Phe  | Glu<br>200 | Leu | Asn | Ser | Glu | Asn<br>205 | Val | Thr | Met | Lys | Val<br>210 |
| Val                          | Ser           | Val | Leu  | Tyr<br>215 | Asn | Val | Thr | Ile | Asn<br>220 | Asn | Thr | Tyr | Ser | Cys<br>225 |
| Met                          | Ile           | Glu | Asn  | Asp<br>230 | Ile | Ala | Lys | Ala | Thr<br>235 | Gly | Asp | Ile | Lys | Val<br>240 |
| Thr                          | Glu           | Ser | Gľu  | Ile<br>245 | Lys | Arg | Arg | Ser | His<br>250 | Leu | Gln | Leu | Leu | Asn<br>255 |
| Ser                          | Lys           | Ala | Ser  | Leu<br>260 | Cys | Val | Ser | Ser | Phe<br>265 | Phe | Ala | Ile | Ser | Trp<br>270 |
| Ala                          | Leu           | Leu | Pro  | Leu<br>275 | Ser | Pro | Tyr | Leu | Met<br>280 | Leu | Lys |     |     |            |
| <210<br><211<br><212<br><213 | > 37<br>> PR' | Г   | apie | n          |     |     |     |     |            |     |     |     |     |            |
| <400<br>Met<br>1             | > 9<br>Val    | Leu | Trp  | Glu<br>5   | Ser | Pro | Arg | Gln | Cys<br>10  | Ser | Ser | Trp | Thr | Leu<br>15  |
| Cys                          | Glu           | Gly | Phe  | Cys<br>20  | Trp | Leu | Leu | Leu | Leu<br>25  | Pro | Val | Met | Leu | Leu<br>30  |
| Ile                          | Val           | Ala | Arg  | Pro<br>35  | Val | Lys | Leu | Ala | Ala<br>40  | Phe | Pro | Thr | Ser | Leu<br>45  |
| Ser                          | Asp           | Cys | Gln  | Thr<br>50  | Pro | Thr | Gly | Trp | Asn<br>55  | Cys | Ser | Gly | Tyr | Asp<br>60  |
| Asp                          | Arg           | Glu | Asn  | Asp<br>65  | Leu | Phe | Leu | Cys | Asp<br>70  | Thr | Asn | Thr | Cys | Lys<br>75  |
| Phe                          | Asp           | Gly | Glu  | Cys<br>80  | Leu | Arg | Ile | Gly | Asp<br>85  | Thr | Val | Thr | Cys | Val<br>90  |

| Cys                              | Gln        | Phe | Lys   | Cys<br>95  | Asn | Asn | Asp | Tyr | Val<br>100 | Pro | Val | Cys | Gly | Ser<br>105 |
|----------------------------------|------------|-----|-------|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|
| Asn                              | Gly        | Glu | Ser   | Tyr<br>110 | Gln | Asn | Glu | Cys | Tyr<br>115 | Leu | Arg | Gln | Ala | Ala<br>120 |
| Cys                              | Lys        | Gln | Gln   | Ser<br>125 | Glu | Ile | Leu | Val | Val<br>130 | Ser | Glu | Gly | Ser | Cys<br>135 |
| Ala                              | Thr        | Asp | Ala   | Gly<br>140 | Ser | Gly | Ser | Gly | Asp<br>145 | Gly | Val | His | Glu | Gly<br>150 |
| Ser                              | Gly        | Glu | Thr   | Ser<br>155 | Gln | Lys | Glu | Thr | Ser<br>160 | Thr | Cys | Asp | Ile | Cys<br>165 |
| Gln                              | Phe        | Gly | Ala   | Glu<br>170 | Cys | Asp | Glu | Asp | Ala<br>175 | Glu | Asp | Val | Trp | Cys<br>180 |
| Val                              | Суз        | Asn | Ile   | Asp<br>185 | Cys | Ser | Gln | Thr | Asn<br>190 | Phe | Asn | Pro | Leu | Cys<br>195 |
| Ala                              | Ser        | Asp | Gly   | Lys<br>200 | Ser | Tyr | Asp | Asn | Ala<br>205 | Cys | Gln | Ile | Lys | Glu<br>210 |
| Ala                              | Ser        | Cys | Gln   | Lys<br>215 | Gln | Glu | Lys | Ile | Glu<br>220 | Val | Met | Ser | Leu | Gly<br>225 |
| Arg                              | Cys        | Gln | Asp   | Asn<br>230 |     | Thr | Thr | Thr | Thr<br>235 | Lys | Ser | Glu | Asp | Gly<br>240 |
| His                              | Tyr        | Ala | Arg   | Thr<br>245 | Asp | Tyr | Ala | Glu | Asn<br>250 | Ala | Asn | Lys | Leu | Glu<br>255 |
| Glu                              | Ser        | Ala | Arg   | Glu<br>260 | His | His | Ile | Pro | Cys<br>265 | Pro | Glu | His | Tyr | Asn<br>270 |
| Gly                              | Phe        | Cys | Met   | His<br>275 | Gly | Lys | Cys | Glu | His<br>280 | Ser | Ile | Asn | Met | Gln<br>285 |
| Glu                              | Pro        | Ser | Cys   | Arg<br>290 | Cys | Asp | Ala | Gly | Tyr<br>295 | Thr | Gly | Gln | His | Cys<br>300 |
| Glu                              | Lys        | Lys | Asp   | Tyr<br>305 | Ser | Val | Leu | Tyr | Val<br>310 | Val | Pro | Gly | Pro | Val<br>315 |
| Arg                              | Phe        | Gln | Tyr   | Val<br>320 | Leu | Ile | Ala | Ala | Val<br>325 | Ile | Gly | Thr | Ile | Gln<br>330 |
| Ile                              | Ala        | Val | Ile   | Cys<br>335 | Val | Val | Val | Leu | Cys<br>340 | Ile | Thr | Arg | Lys | Cys<br>345 |
| Pro                              | Arg        | Ser | Asn   | Arg<br>350 | Ile | His | Arg | Gln | Lys<br>355 | Gln | Asn | Thr | Gly | His<br>360 |
| Tyr                              | Ser        | Ser | Asp   | Asn<br>365 | Thr | Thr | Arg | Ala | Ser<br>370 | Thr | Arg | Leu | Ile |            |
| <210:<br><211:<br><212:<br><213: | 454<br>PRI | :   | ıpier | 1          |     |     |     |     |            |     |     |     |     |            |

<400> 10 Met Glu Ser Ile Ser Met Met Gly Ser Pro Lys Ser Leu Ser Glu

| 1   |     |     |     | 5          |     |     |     |     | 10         |     |     |     |     | 15         |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|
| Thr | Cys | Leu | Pro | Asn<br>20  | Gly | Ile | Asn | Gly | Ile<br>25  | Lys | Asp | Ala | Arg | Lys<br>30  |
| Val | Thr | Val | Gly | Val<br>35  | Ile | Gly | Ser | Gly | Asp<br>40  | Phe | Ala | Lys | Ser | Leu<br>45  |
| Thr | Ile | Arg | Leu | Ile<br>50  | Arg | Суѕ | Gly | Tyr | His<br>55  | Val | Val | Ile | Gly | Ser<br>60  |
| Arg | Asn | Pro | Lys | Phe<br>65  | Ala | Ser | Glu | Phe | Phe<br>70  | Pro | His | Val | Val | Asp<br>75  |
| Val | Thr | His | His | Glu<br>80  | Asp | Ala | Leu | Thr | Lys<br>85  | Thr | Asn | Ile | Ile | Phe<br>90  |
| Val | Ala | Ile | His | Arg<br>95  | Glu | His | Tyr | Thr | Ser<br>100 | Leu | Trp | Asp | Leu | Arg<br>105 |
| His | Leu | Leu | Val | Gly<br>110 | Lys | Ile | Leu | Ile | Asp<br>115 | Val | Ser | Asn | Asn | Met<br>120 |
| Arg | Ile | Asn | Gln | Tyr<br>125 | Pro | Glu | Ser | Asn | Ala<br>130 | Glu | Tyr | Leu | Ala | Ser<br>135 |
| Leu | Phe | Pro | Asp | Ser<br>140 | Leu | Ile | Val | Lys | Gly<br>145 | Phe | Asn | Val | Val | Ser<br>150 |
| Ala | Trp | Ala | Leu | Gln<br>155 | Leu | Gly | Pro | Lys | Asp<br>160 | Ala | Ser | Arg | Gln | Val<br>165 |
| Tyr | Ile | Cys | Ser | Asn<br>170 | Asn | Ile | Gln | Ala | Arg<br>175 | Gln | Gln | Val | Ile | Glu<br>180 |
| Leu | Ala | Arg | Gln | Leu<br>185 | Asn | Phe | Ile | Pro | Ile<br>190 | Asp | Leu | Gly | Ser | Leu<br>195 |
| Ser | Ser | Ala | Arg | Glu<br>200 | Ile | Glu | Asn | Leu | Pro<br>205 | Leu | Arg | Leu | Phe | Thr<br>210 |
| Leu | Trp | Arg | Gly | Pro<br>215 | Val | Val | Val | Ala | Ile<br>220 | Ser | Leu | Ala | Thr | Phe<br>225 |
| Phe | Phe | Leu | Tyr | Ser<br>230 | Phe | Val | Arg | Asp | Val<br>235 | Ile | His | Pro | Tyr | Ala<br>240 |
| Arg | Asn | Gln | Gln | Ser<br>245 | Asp | Phe | Tyr | Lys | 0 - 0      | Pro | Ile | Glu | Ile | Val<br>255 |
| Asn | Lys | Thr | Leu | Pro<br>260 | Ile | Val | Ala | Ile | Thr<br>265 | Leu | Leu | Ser | Leu | Val<br>270 |
| Tyr | Leu | Ala | Gly | Leu<br>275 | Leu | Ala | Ala | Ala | Tyr<br>280 | Gln | Leu | Tyr | Tyr | Gly<br>285 |
| Thr | Lys | Tyr | Arg | Arg<br>290 | Phe | Pro | Pro | Trp | Leu<br>295 | Glu | Thr | Trp | Leu | Gln<br>300 |
| Cys | Arg | Lys | Gln | Leu<br>305 | Gly | Leu | Leu | Ser | Phe<br>310 | Phe | Phe | Ala | Met | Val<br>315 |
| His | Val | Ala | Tyr | Ser<br>320 | Leu | Cys | Leu | Pro | Met<br>325 | Arg | Arg | Ser | Glu | Arg<br>330 |

Tyr Leu Phe Leu Asn Met Ala Tyr Gln Gln Val His Ala Asn Ile 335 . Glu Asn Ser Trp Asn Glu Glu Glu Val Trp Arg Ile Glu Met Tyr 350 Ile Ser Phe Gly Ile Met Ser Leu Gly Leu Leu Ser Leu Leu Ala 370 365 Val Thr Ser Ile Pro Ser Val Ser Asn Ala Leu Asn Trp Arg Glu Phe Ser Phe Ile Gln Ser Thr Leu Gly Tyr Val Ala Leu Leu Ile 395 400 Ser Thr Phe His Val Leu Ile Tyr Gly Trp Lys Arg Ala Phe Glu 410 415 Glu Glu Tyr Tyr Arg Phe Tyr Thr Pro Pro Asn Phe Val Leu Ala Leu Val Leu Pro Ser Ile Val Ile Leu Asp Leu Leu Gln Leu Cys 445 Arg Tyr Pro Asp